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# **Influenza vaccination and risk of stroke: self-controlled case-series study**

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# Summary of talk

- Background and motivation
- Previous studies
- Study aim and method
- Analysis and Results
- Conclusions

# Background

- Stroke is a major cause of death and long term illness
- 5% of UK population are affected, around 130 thousand suffer a new or recurrent stroke each year
- Common risk factors such as age, gender, smoking, diabetes .., don't account for all the stroke cases
- Emerging evidence shows that respiratory infections and incidence of strokes may be related

# Previous studies

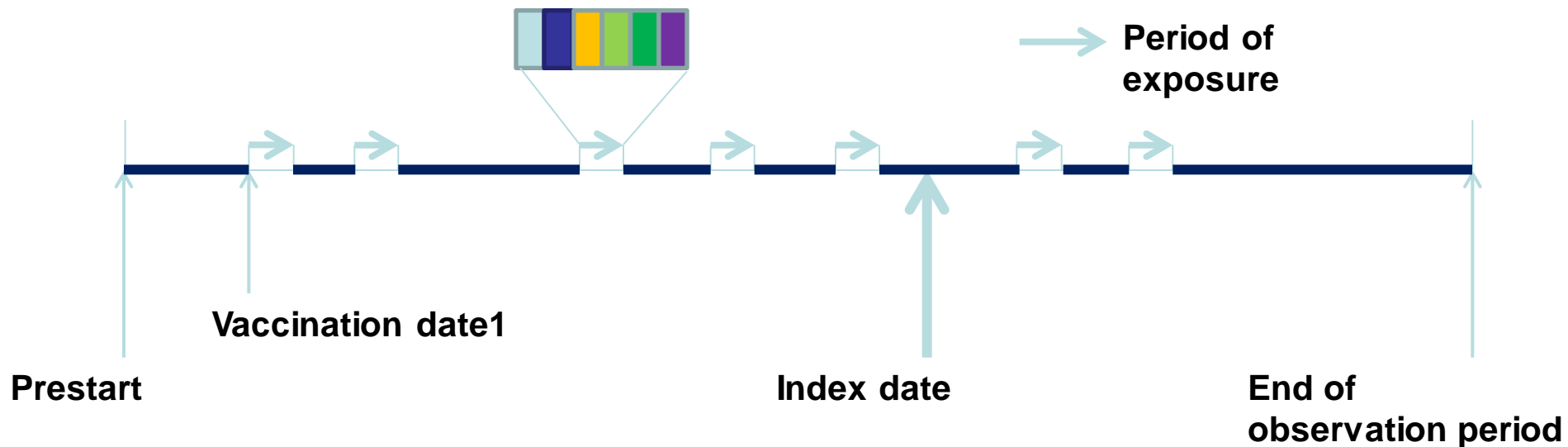
- Contradictory evidence: Small study size
- Design Bias: recall, therapeutic
- Confounding: 'healthy user effect', missing different treatments and differences in health behaviours in vaccinees.

# Study aim

To investigate whether influenza vaccination was associated with a reduced risk of stroke.

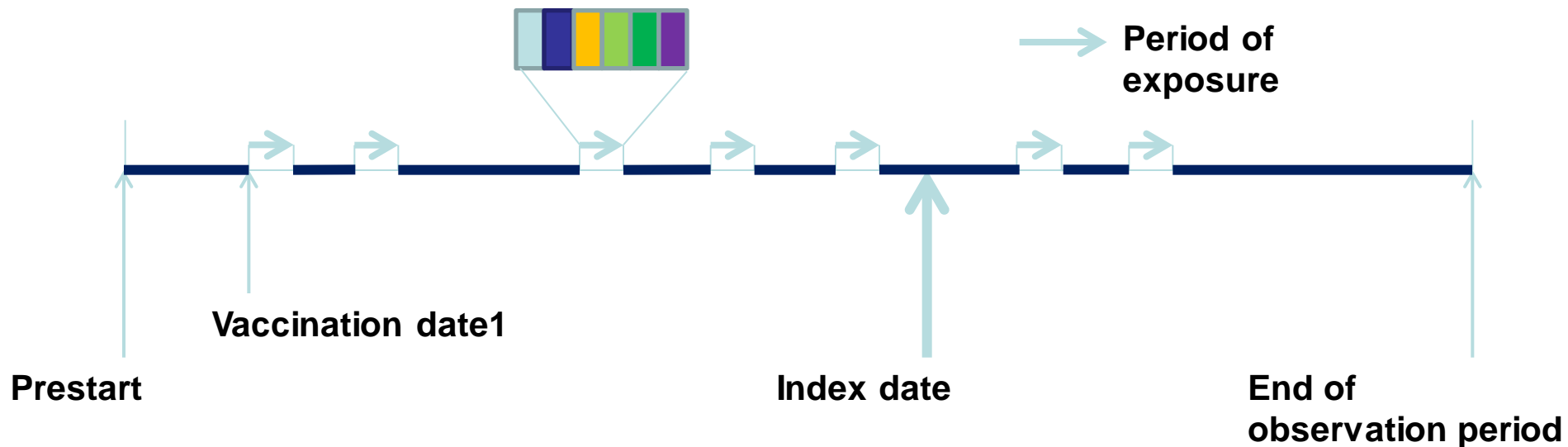
# Method

- Vaccination season from 01 Sept 2001-31 Aug 2009



# Method

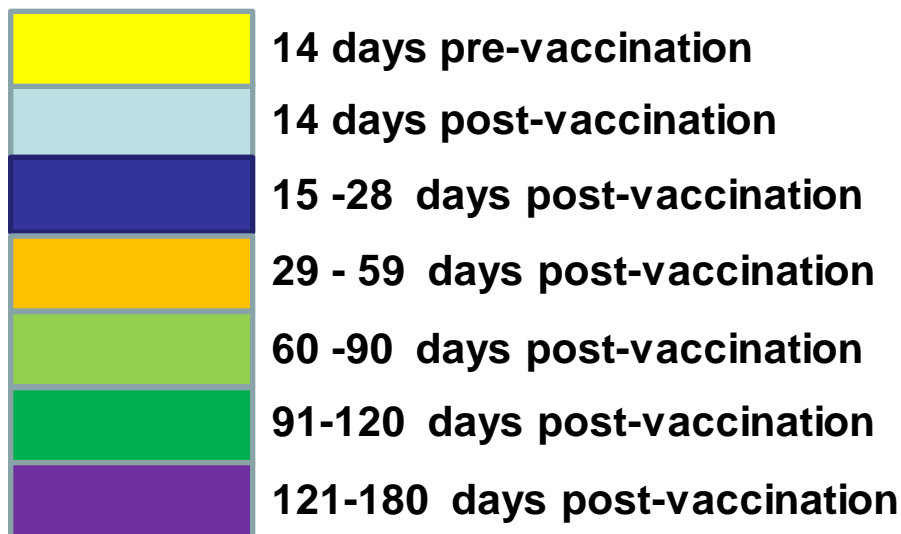
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# Method

- Vaccination season from 01 Sept 2001-31 Aug 2009

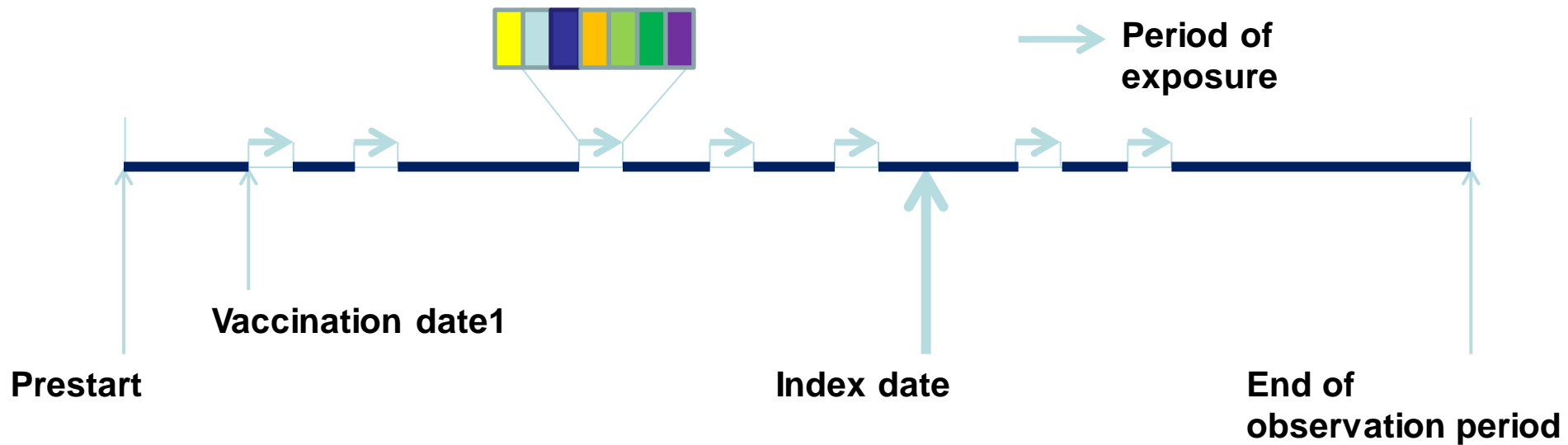
Vaccination periods:





# Method

- Exposure-Base line cut points



# Method

- **Case:** medical diagnostic Read/OXMIS codes for first stroke entered by GP
- **Index date:** first date when GP recorded stroke code (fatal/non-fatal) in clinical/referral record
- In the case-series method the Cases act as Controls

# Method

- Cut-off points for risk periods and seasons were calculated for each year.
- There were eight pre-defined risk periods including: the baseline period for each interval: 1-14 days before vaccination and; 1-14 days; 15-28 days; 29-59 days; 60-90 days; 91-120 days; 121-180 days post vaccination.

# Method

- 1-14 days pre-vaccination considered as a separate interval: a stroke event occurring during this period is likely to affect the subsequent likelihood of receiving an influenza vaccination.
- Seasonality was included by dividing the risk periods into one of four quarterly seasons: Sept. to Nov.; Dec. to Feb.; March to May and June to Aug.

# Method

- The vaccination timings were split into:

Early (1 September to 15 November) and

Late (16 November to 30 April) vaccinations.

# Analysis

- The incidence rate of stroke in fixed time periods after vaccination was compared with the incidence rate during a baseline period.
- Statistical modelling with conditional Poisson regression in Stata 12 was employed to compute incidence rate ratios (IRR).

# Descriptive statistics

- 21,981 first cases of stroke within the observation period
- 4,128 cases that either did not receive influenza vaccination or had a stroke diagnosis on or before the vaccination date were excluded

# Descriptive statistics

- 17,853 cases of stroke considered for the final analysis.
- 52.8% (9,424) females and 47.2% (8,429) males.
- The median age at first stroke diagnosis was 75 years (interquartile range 68-81 years).
- 85.7% were aged 65 and over.



# Main results

## Association between influenza vaccination and stroke

Risk period	Number of cases		Time at risk (person years)	IRR	Adjusted 95% CI
	N	%			
base line period	10001	54.2	53738	1.00	-
Pre Vac 1-14 days	334	3.0	2983	0.55	0.49 - 0.61
Post Vac 1-14 days	462	3.5	3421	0.63	0.57 - 0.69
15-28 days	552	3.4	3417	0.76	0.70 - 0.84
29-59 days	1268	7.6	7545	0.83	0.77 - 0.89
60-90 days	1388	7.6	7506	0.95	0.88 - 1.03
91-120 days	1363	7.3	7212	0.99	0.92 - 1.06
121-180 days	2485	13.4	13266	1.02	0.97 - 1.08

<sup>a</sup> Adjusted for seasonality

<sup>b</sup> IRR incidence rate ratios.

<sup>c</sup> Baseline is between 180 days or 30th of April (whichever came first) after vaccination and 14 days prior to next vaccination

# Main results

## Seasonally adjusted IRR by gender and timing of vaccination

Risk period (days)	Gender				Vaccination timing			
	Female		Male		Early (1 September to 15 November)		Late (16 November to 30 April)	
	IRR	Adjusted 95% CI	IRR	Adjusted 95% CI	IRR** p<0.01	Adjusted 95% CI	IRR p>0.01	Adjusted 95% CI
Base line period	1	-	1	-	1	-	1	-
Pre-vaccination 1-14 days	0.54	0.46 - 0.64	0.65	0.47 - 0.65	0.55	0.55 - 0.68	0.45	0.17 - 1.21
Post-vaccination 1-14 days	0.6	0.52 - 0.69	0.66	0.58 - 0.76	0.62	0.57 - 0.69	0.74	0.38 –1.45
15-28 days	0.79	0.70 - 0.89	0.74	0.64 - 0.84	0.75	0.69 - 0.83	1.16	0.68 – 2.00
29-59 days	0.78	0.71 - 0.86	0.88	0.80 - 0.97	0.83	0.77 - 0.88	1.11	0.76 –1.63
60-90 days	0.95	0.86 - 1.05	0.96	0.86 - 1.07	0.96	0.89 - 1.03	1.08	0.72 –1.61
91-120 days	0.93	0.84 - 1.03	1.07	0.96 - 1.18	1.00	0.93 - 1.08	0.67	0.38 –1.19
121-180 days	1.01	0.94 - 1.09	1.04	0.97 - 1.13	1.03	0.97 - 1.08	0.82	0.30 –2.18

All IRRs are adjusted for seasonality

# Study strengths and limitations

- We used a large, representative and robust research database with sufficient power to detect effects with precision.
- Selection bias was minimized by including all cases of stroke within the selected time period.
- Confounders are taken into account naturally assuming that they don't change over the observational period.

# Study strengths and limitations

- Since the method assumes that the confounders do not change over the observational period: it does not account for **within-person** confounding due to confounders varying over the observational period.
- We counter this effect by restricting the observational period at first vaccination date.

# Conclusion

- Influenza vaccination in the preceding season is associated with a reduction in incidence of stroke. This study supports previous studies which have shown a beneficial association of influenza vaccination in stroke prevention.

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# Thank you

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